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DATE: Thursday, February 10, 2005

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☐	L3	(HSV1 or herpesvir$4) same VP22 and (microtub$ or actin or chromatin)	26
☐	L2	(HSV1 or herpesvir$4) same VP22 and VP22 same (transport$ or carr$ or deliver$ or fusion or microtub$)	52
☐	L1	(HSV1 or herpesvir$4) same VP22 and VP22 same (transport$ or carr$ or fusion or microtub$)	50

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#15	Search **#12 AND #13** Field: **Title/Abstract,** Limits: **Publication Date to 1999**	17:25:50	7
#14	Search **#12 AND #13** Field: **Title/Abstract**	17:25:36	44
#13	Search **VP22 AND (herpes* or virus)** Field: **Title/Abstract**	17:25:21	97
#12	Search **VP22 AND (carr* or deliver* or transport*)** Field: **Title/Abstract**	17:25:03	59
#11	Search **#10 AND #7**	17:24:45	67
#10	Search **VP22 AND (carr* or deliver* or transport*)**	17:24:32	70
#9	Search **VP22 AND (cytoskel* or actin or microtub*)**	17:23:56	11
#8	Search **VP22 AND (actin or microtub*)**	17:23:44	10
#7	Search **VP22 AND (herpes* or virus)**	17:23:28	121

Clear History

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FILE 'HOME' ENTERED AT 17:54:25 ON 10 FEB 2005

L1 269 VP22 (S) (HERPESVIR#### OR HERPES OR HSV OR HSV1) (P) (MICROTUB? OR DELIVER? OR TRANSPORT? OR CARR?)

L2 301 VP22 (S) (HERPESVIR#### OR HERPES OR HSV OR HSV1) AND VP22 (P) (MICROTUB? OR DELIVER? OR TRANSPORT? OR CARR?)

(FILE 'HOME' ENTERED AT 17:54:25 ON 10 FEB 2005)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 17:54:58 ON 10 FEB 2005

L1 269 S VP22 (S) (HERPESVIR#### OR HERPES OR HSV OR HSV1) (P) (MICROT
L2 301 S VP22 (S) (HERPESVIR#### OR HERPES OR HSV OR HSV1) AND VP22 (P
L3 50 S L2 AND (ACTIN OR MICROTUB?)
L4 114 DUP REM L2 (187 DUPLICATES REMOVED)
L5 14 S L3 AND L4
L6 3 S L5 AND PY<1999
L7 106 S L4 AND (DELIVER? OR TRANSPORT? OR CARR?)
L8 88 S L7 AND VP22 (S) (DELIVER? OR TRANSPORT? OR CARR?)
L9 9 S L8 AND PY<1999
L10 7 S L9 NOT L5

L6 ANSWER 1 OF 3 MEDLINE on STN
AN 1998325159 MEDLINE
DN PubMed ID: 9658087
TI **Herpes** simplex virus type 1 tegument protein **VP22** induces the stabilization and hyperacetylation of **microtubules**.
AU Elliott G; O'Hare P
CS Marie Curie Research Institute, Oxted, Surrey RH8 OTL, United Kingdom.. g.elliott@mcri.ac.uk
SO Journal of virology, **(1998 Aug)** 72 (8) 6448-55.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199808
ED Entered STN: 19980817
Last Updated on STN: 19980817
Entered Medline: 19980805
AB The role of the **herpes** simplex virus type 1 tegument protein **VP22** during infection is as yet undefined. We have previously shown that **VP22** has the unusual property of efficient intercellular **transport**, such that the protein spreads from single expressing cells into large numbers of surrounding cells. We also noted that in cells expressing **VP22** by transient transfection, the protein localizes in a distinctive cytoplasmic filamentous pattern. Here we show that this pattern represents a colocalization between **VP22** and cellular **microtubules**. Moreover, we show that **VP22** reorganizes **microtubules** into thick bundles which are easily distinguishable from nonbundled **microtubules**. These bundles are highly resistant to **microtubule**-depolymerizing agents such as nocodazole and incubation at 4 degreesC, suggesting that **VP22** has the capacity to stabilize the **microtubule** network. In addition, we show that the **microtubules** contained in these bundles are modified by acetylation, a marker for **microtubule** stability. Analysis of infected cells by both immunofluorescence and measurement of **microtubule** acetylation further showed that colocalization between **VP22** and **microtubules**, and induction of **microtubule** acetylation, also occurs during infection. Taken together, these results suggest that **VP22** exhibits the properties of a classical **microtubule** -associated protein (MAP) during both transfection and infection. This is the first demonstration of a MAP encoded by an animal virus.

L6 ANSWER 2 OF 3 MEDLINE on STN
AN 97160843 MEDLINE
DN PubMed ID: 9008163
TI Intercellular trafficking and protein delivery by a herpesvirus structural protein.
AU Elliott G; O'Hare P
CS Marie Curie Research Institute, The Chart, Osted, Surrey, United Kingdom.
SO Cell, **(1997 Jan 24)** 88 (2) 223-33.
Journal code: 0413066. ISSN: 0092-8674.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199702
ED Entered STN: 19970305
Last Updated on STN: 19980206
Entered Medline: 19970218

AB We show that the **HSV**-1 structural protein **VP22** has the remarkable property of intercellular **transport**, which is so efficient that following expression in a subpopulation the protein spreads to every cell in a monolayer, where it concentrates in the nucleus and binds chromatin. **VP22** movement was observed both after **delivery** of DNA by transfection or microinjection and during virus infection. Moreover, we demonstrate that **VP22** trafficking occurs via a nonclassical Golgi-independent mechanism. Sensitivity to cytochalasin D treatment suggests that **VP22** utilizes a novel trafficking pathway that involves the **actin** cytoskeleton. In addition, we demonstrate intercellular **transport** of a **VP22** fusion protein after endogenous synthesis or exogenous application, indicating that **VP22** may have potential in the field of protein **delivery**.

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:672582 CAPLUS
DN 129:272099
TI **Herpesvirus VP22** proteins binding to and stabilization of **microtubules**
IN Elliott, Gillian Daphne
PA Phogen Limited, UK
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9842742	A1	19981001	WO 1998-GB873	19980323 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2283794	AA	19981001	CA 1998-2283794	19980323 <--
	AU 9867393	A1	19981020	AU 1998-67393	19980323 <--
	EP 971953	A1	20000119	EP 1998-912613	19980323
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001520521	T2	20011030	JP 1998-545227	19980323
	US 2002128174	A1	20020912	US 1999-381211	19990917
	MX 9908620	A	20000731	MX 1999-8620	19990920
PRAI	GB 1997-5903	A	19970321		
	WO 1998-GB873	W	19980323		

AB **Herpesviral VP22** proteins (product of **herpes** simplex virus type 1 UL49 gene) are used to modify cell structure and cell division, by their newly found property of binding to **microtubules** in cells. **VP22** stabilizes **microtubules** against the action of depolymg. agents in a similar way to the known **microtubule** binding agent, taxol. The region of **herpes** simplex virus type 1 **VP22** involved in **microtubule** associated lies between residues 119 and 192; deletions in this region disrupt the structure of the **VP22** determinant responsible for the **microtubule** binding. Uses of **VP22** to exploit this property include stabilization of animal cellular **microtubules** in vivo and in vitro, e.g. to retard or arrest cell division or induce cell death. The **microtubule** binding function of **VP22**

can be exploited by reagent use in vitro to study **microtubules** or the cell cycle, particularly at cell division, and pharmaceutically to retard or arrest cell division of cells such as neoplastic cells or protozoal parasite cells in vitro or in vivo.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 1 OF 7 MEDLINE on STN
AN 1998254727 MEDLINE
DN PubMed ID: 9592391
TI Intercellular **delivery** of functional p53 by the **herpesvirus** protein **VP22**.
CM Comment in: Nat Biotechnol. 1998 May;16(5):418-20. PubMed ID: 9592386
AU Phelan A; Elliott G; O'Hare P
CS Marie Curie Research Institute, Surrey, UK.
SO Nature biotechnology, **(1998 May)** 16 (5) 440-3.
Journal code: 9604648. ISSN: 1087-0156.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199808
ED Entered STN: 19980903
Last Updated on STN: 19980903
Entered Medline: 19980824
AB The **herpes** simplex virus type 1 (**HSV**-1) virion protein **VP22** exhibits the remarkable property of intercellular trafficking whereby the protein spreads from the cell in which it is synthesized to many surrounding cells. In addition to having implications for protein trafficking mechanisms, this function of **VP22** might be exploited to overcome a major hurdle in gene therapy, i.e., efficient **delivery** of genes and gene products. We show that chimeric polypeptides, consisting of **VP22** linked to the entire p53 protein, retain their ability to spread between cells and accumulate in recipient cell nuclei. Furthermore the p53-**VP22** chimeric protein efficiently induces apoptosis in p53 negative human osteosarcoma cells resulting in a widespread cytotoxic effect. The intercellular **delivery** of functional p53-**VP22** fusion protein is likely to prove beneficial in therapeutic strategies based on restoration of p53 function. These results, demonstrating intracellular **transport** of large functional proteins, indicate that **VP22** **delivery** may have applications in gene therapy.

L10 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:804203 CAPLUS
DN 130:51339
TI **Herpes** simplex virus **VP22** for treatment and prevention of infection
IN Burke, Rae Lyn; Tigges, Michael A.
PA Chiron Corp., USA
SO PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9855145	A1	19981210	WO 1998-US10664	19980526 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2291010	AA	19981210	CA 1998-2291010	19980526 <--

AU 9875979 A1 19981221 AU 1998-75979 19980526 <--
EP 984790 A1 20000315 EP 1998-923762 19980526
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2002503251 T2 20020129 JP 1999-502530 19980526
US 2003017174 A1 20030123 US 1998-84669 19980526
US 6635258 B2 20031021
PRAI US 1997-47359P P 19970602
WO 1998-US10664 W 19980526
AB The authors disclose the cloning and characterization of **herpes** simplex virus (**HSV**) **VP22** polypeptide. **VP22** was capable of eliciting a cellular immune response and methods for treating and preventing **HSV** infections are disclosed. Vaccine containing **VP22** can also include addnl. **HSV** polypeptides, such as envelope glycoproteins.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:719298 CAPLUS
DN 130:7395
TI Modified baculovirus containing exogenous nucleic acid for **delivery** of said nucleic acid to hepatocytes
IN McGarvey, Michael Joseph; Thomas, Howard Christopher
PA Imperial College Innovations Ltd., UK
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9848842	A1	19981105	WO 1998-GB1249	19980429 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9872217	A1	19981124	AU 1998-72217	19980429 <--
EP 979106	A1	20000216	EP 1998-919340	19980429
R: BE, DE, ES, FR, GB, IT, NL				
US 2001000228	A1	20010412	US 2000-729856	20001206
PRAI GB 1997-8698	A	19970429		
WO 1998-GB1249	W	19980429		
US 1999-428532	B1	19991028		

AB Modified baculovirus particles containing prophylactic and/or therapeutic nucleic acids are provided, together with their use in treating liver conditions such as viral infections.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:661575 CAPLUS
DN 130:34572
TI Intercellular trafficking of VP22-GFP fusion proteins is not observed in cultured mammalian cells
AU Fang, B.; Xu, B.; Koch, P.; Roth, J. A.
CS Section Molecular Oncology, Dep. Thoracic and Cardiovascular Surgery,

University Texas MD Anderson Cancer Center, Houston, TX, 77030, USA
SO Gene Therapy (**1998**), 5(10), 1420-1424
CODEN: GETHEC; ISSN: 0969-7128
PB Stockton Press
DT Journal
LA English
AB **Herpes** simplex virus type 1 (**HSV-1**) **VP22** was recently reported to mediate intercellular trafficking of a protein fused to the C-terminus of **VP22**. To explore the application of such trafficking, we constructed plasmids expressing green fluorescent protein (GFP) fused to the C-terminus of either wild-type VP22 or a 160 amino acid peptide from VP22. In vitro studies showed that the majority of both fused proteins were localized to the nuclei of transfected cells. Quant. anal. of GFP-pos. cells, however, showed no significant increase in intercellular protein trafficking for cells transfected with either fusion protein compared with a lacZ-expressing plasmid. Our results suggest that the use of **HSV**-1 **VP22** for mediating intercellular trafficking of transgene products is limited.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:527442 CAPLUS
DN 129:132838
TI Fusion proteins containing **herpesvirus VP22** for intracellular and intercellular **transport** and their uses
IN O'Hare, Peter Francis Joseph; Elliott, Gillian Daphne
PA Marie Curie Cancer Care, UK
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9832866	A1	19980730	WO 1998-GB207	19980123 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 6017735	A	20000125	US 1998-12126	19980122
	CA 2278002	AA	19980730	CA 1998-2278002	19980123 <--
	AU 9856749	A1	19980818	AU 1998-56749	19980123 <--
	AU 735830	B2	20010719		
	EP 961829	A1	19991208	EP 1998-900953	19980123
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001508304	T2	20010626	JP 1998-531733	19980123
	US 6251398	B1	20010626	US 1999-395344	19990913
	US 2002106378	A1	20020808	US 2001-800433	20010305
	AU 759858	B2	20030501	AU 2001-81504	20011019
	US 2004197346	A1	20041007	US 2003-654869	20030903
PRAI	GB 1997-1363	A	19970123		
	GB 1997-16398	A	19970801		
	US 1998-12126	A1	19980122		
	AU 1998-56749	A3	19980123		
	WO 1998-GB207	W	19980123		

US 1999-395344 A1 19990913
US 2001-800433 B1 20010305

AB Coupled polypeptides and fusion polypeptides for intracellular **transport**, and their preparation and use, include (i) an amino acid sequence with the **transport** function of **herpesviral** **VP22** protein (or homolog, e.g. from varicella zoster virus, bovine **herpesvirus**, or MDV) and (ii) another protein sequence selected from (a) proteins for cell cycle control, (b) suicide proteins, (c) antigenic sequences or antigenic proteins from microbial and viral antigens and tumor antigens, (d) immunomodulating proteins, and (e) therapeutic proteins. The coupled proteins can be used for intracellular **delivery** of protein sequences (ii), to exert the corresponding effector function in the target cell, and the fusion polypeptides can be expressed from corresponding polynucleotides, vectors and host cells. Thus, the **VP22**-p53 fusion construct was generated by cloning a full-length p53 PCR fragment C-terminal to **VP22** into a unique Bam site of plasmid vector, keeping both **VP22** and the cytomegalovirus epitope in frame. This vector generates a fusion protein of .apprx.90 kDa when expressed in COS-1 cells, with very little protein degradation as judged by Western blot anal. When tested for **delivery** by intercellular trafficking, the fusion protein appears to function exactly as **VP22** alone. P53-neg. osteosarcoma cells were transfected with naked DNA expressibly encoding the **VP22**-p53, and the transfected cells showed ability to undergo apoptosis, unlike control cells, indicating that the **VP22**-p53 fusion protein retains the functionality of p53.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:226808 CAPLUS
DN 126:208206
TI Viral proteins rapidly **transported** intercellularly from host cells manufacturing them and their uses
IN O'Hare, Peter Francis Joseph; Elliott, Gillian Daphne
PA O'Hare, Peter Francis Joseph, UK; Elliott, Gillian Daphne
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9705265	A1	19970213	WO 1996-GB1831	19960725 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
CA 2227786	AA	19970213	CA 1996-2227786	19960725 <--
AU 9666239	A1	19970226	AU 1996-66239	19960725 <--
AU 705563	B2	19990527		
EP 845043	A1	19980603	EP 1996-925874	19960725 <--
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CN 1208438	A	19990217	CN 1996-195845	19960725
BR 9610058	A	19990727	BR 1996-10058	19960725
JP 11510386	T2	19990914	JP 1996-507359	19960725
ZA 9606406	A	19970219	ZA 1996-6406	19960726 <--
US 6184038	B1	20010206	US 1998-11073	19980126

	US 2002039765	A1	20020404	US 2001-773430	20010131
	US 6521455	B2	20030218		
	US 2003219859	A1	20031127	US 2002-259198	20020927
PRAI	GB 1995-15568	A	19950728		
	GB 1996-1570	A	19960126		
	WO 1996-GB1831	W	19960725		
	US 1998-11073	XX	19980126		
	US 2001-773430	A1	20010131		

AB Viral proteins that are rapidly exported from an infected host cell and that spread rapidly through monolayer cell cultures, in particular **herpes** simplex virus I **VP22** protein and homologs, are characterized for use in the distribution of therapeutic proteins to target populations of cells. This protein has applications in gene therapy and methods of targeting agents to cells where targeting at high efficiency is required. Immunofluorescence studies showed that **VP22** either accumulated around the nucleus of a cell or it was excluded from the cell and passed through the cytoplasm to adjacent cells and then spread rapidly to surrounding cells. Deletion anal. indicated that a C-terminal 34 amino acid region of the protein was essential for this **transport**. Uptake of **VP22** protein added to the medium as cell lysates is very rapid and is temperature-insensitive. **VP22** fusion proteins with green fluorescent protein showed that proteins of up to 32 kilodaltons can be disseminated as fusion proteins with **VP22**.

L10 ANSWER 7 OF 7 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AN 95218940 EMBASE

DN 1995218940

TI PREPs: Herpes simplex virus type 1-specific particles produced by infected cells when viral DNA replication is blocked.

AU Dargan D.J.; Patel A.H.; Subak-Sharpe J.H.

CS Virology Unit, Medical Research Council, University of Glasgow, Church St.,Glasgow G11 5JR, United Kingdom

SO Journal of Virology, (1995) 69/8 (4924-4932).
ISSN: 0022-538X CODEN: JOVIAM

CY United States

DT Journal; Article

FS 004 Microbiology

LA English

SL English

AB **Herpes** simplex virus (**HSV**)-infected cells produce not only infectious nucleocapsid-containing virions bat also virion-related noninfectious light particles (L-particles) composed of the envelope and tegument components of the virus particle (J. F. Szilagyi and C. Cunningham, J. Gen. Virol. 62:661- 668, 1991). We show that BHK and MeWO cells infected either with wild-type (WT) **HSV** type 1 (**HSV**-1) in the presence of viral DNA replication inhibitors (cytosine-β-D-arabinofuranoside, phosphonoacetic acid, and acycloguanosine) or with a viral DNA replication-defective mutant of **HSV**-1 (ambUL8) synthesize a new type of virus-related particle that is morphologically similar to an L- particle but differs in its relative protein composition. These novel particles we term pre-viral DNA replication enveloped particles (PREPs). The numbers of PREPs released into the culture medium were of the same order as those of L-particles from control cultures. The particle/PFU ratios of different PREP stocks ranged from 6 x 105 to 3.8 x 108, compared with ratios of 3 x 103 to 1 x 104 for WT L-particle stocks. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis and Western immunoblot analyses revealed that true late proteins, such as 273K (VP1-2), 82/81K (VP13/14), and gC (VP8), were greatly reduced or absent in PREPs and that gD (VP17) and 40K proteins

were also underrepresented. In contrast, the amounts of proteins 175K (VP4; IE3), 92/91K (VP11/12), 38K (**VP22**), and gE (with BHK cells) were increased. The actual protein composition of PREPs showed some cell line- dependent differences, particularly in the amount of gE. PREPs were biologically competent and **delivered** functional Vmw65 (VP16; αTIF) to target cells, but the efficiency of complementation of the **HSV**-1 (strain 17) mutant in 1814 was 10 to 30% of that of WT L-particles.